PHILIPPINE COLLEGE OF HEMATOLOGY AND TRANSFUSION MEDICINE CONSENSUS ON CONVALESCENT PLASMA THERAPY FOR COVID-19

As proposed by the Convalescent Plasma Therapy Special Interest Group
Interest Group Lead: Teresita Dumagay, MD
Rapid Review Group Members: Joy De Castro, MD; Deonne Gauiran, MD; Flordeluna Mesina, MD; Frances Sapinoso, MD
Center Representatitves: Heidi Abduhraman, MD; Alma Calavera, MD; Kimberley Cutiyog, MD; Marisol Gallemaso, MD; Francis Lopez, MD; Susie Ponce, MD; Pia Angela Receno, MD ; Jesus Relos, MD; Larnie Vencer, MD

Convalescent plasma therapy (CPT) is one of the experimental treatments tapped during the COVID-19 pandemic. It is currently being used both in the setting of clinical trials and compassionate use. Most recent trials have shown benefit of its use in certain defined populations and if units with high titer antibody levels are used. High titer antibody level units have been defined as >18.45 (S/Co VITROS CLIA).

Given this and other emerging data from international and local centers, it is the recommendation of the Philippine College of Hematology and Transfusion Medicine to amend current local guidelines to streamline and maximize CPT benefits. The following are the proposed specific changes on the CPT guidelines.

Convalescent Plasma Therapy Program

- It is recommended that a hematologist be part of the hospital CPT program.
- It is recommended that a hematologist be part of the clinical team managing a patient receiving CPT.
- Guidelines maybe revised when more data from clinical trials is made available.

Donor Eligibility Criteria

- Passed the standard DOH-prescribed donor history questionnaires, where applicable with an age range of 18 to 65 years old
- Recovered from COVID-19 with the following order of preference for donors of CP:

1st priority	• Previously diagnosed with COVID-19 by SARS-CoV-2 RT-PCR • Absence of any clinical evidence of COVID-19 for at least **14 days** as determined by a licensed physician, preferably but not limited to an Infectious Disease Specialist who will issue medical clearance as part of documentary requirement • With at least 1 negative SARS-CoV-2 RT-PCR result done on recovery
2nd priority	• Previously diagnosed with COVID-19 by SARS-CoV-2 RT-PCR • Absence of any clinical evidence of COVID-19 for at least **14 days** as determined by a licensed physician, preferably but not limited to an Infectious Disease Specialist who will issue medical clearance as part of documentary requirement • Even without a negative SARS-CoV-2 RT-PCR result done on recovery
3rd priority	• No SARS-CoV-2 RT-PCR test done to document disease • Absence of any clinical evidence of COVID-19 for at least **14 days** as determined by a licensed physician, preferably but not limited to an Infectious Disease Specialist who will issue medical clearance as part of documentary requirement • Positive result for anti-SARS-CoV-2 IgG antibody-based test

- Negative for anti-HLA antibodies for donors with prior transfusions and female donors with history of pregnancy
- Meet additional laboratory parameters:
  - Hemoglobin greater than or equal to 12.5 g/dL for females or 13.5 g/dL for males
  - Platelet count more than or equal to 150,000/mm^3
- Must have signed informed consent for donation

Convalescent Plasma Units Eligible for use

- Collected plasma units should be tested for antibody levels.
- The following are the recommended antibody titer levels per testing kit manufacturer:

Tests Acceptable for Use in the Manufacture of High Titer COVID-19 Convalescent Plasma		
Manufacturer (listed alphabetically)	**Assay**	**Qualifying Result**
Abbott	SARS-CoV-2 IgG (ARCHITECT and Alinityi)	Index (S/C) ≥ 4.5
Beckman Coulter	Access SARS-CoV-2 IgG	S/CO ≥ 3.3
EUROIMMUN	Anti-SARS-CoV-2 ELISA (IgG)	Ratio ≥ 3.5
GenScript	cPass SARS-CoV-2 Neutralization Antibody Detection Kit	Inhibition ≥ 68%
Kantaro	COVID-SeroKlir, Kantaro Semi-Quantitative SARS-CoV-2 IgG Antibody Kit	Spike ELISA > 47 AU/mL
Mount Sinai	COVID-19 ELISA IgG	Spike ELISA titer ≥ 1:2880
Ortho	VITROS Anti-SARS-CoV-2 IgG	S/C ≥ 9.5
Roche	Elecsys Anti-SARS-CoV-2 S	≥ 132 U/mL
Siemens	ADVIA Centaur SARS-CoV-2 IgG (COV2G)	Index ≥ 4.8

- If manufacturer is not listed above, cut-off levels for antibody titers should be equal to values specified (any 1 of the previously identified manufacturer). Cut-off levels should have documented validation.
- Use of plasma units with antibody titer levels below these cut off values is discouraged.

Vaccination and Donation

- Individuals who have never been infected with COVID-19 and have received a COVID-19 vaccine are not eligible to donate convalescent plasma
- Recovered COVID-19 patients who are eligible to donate and also receive an investigational, authorized or licensed COVID-19 vaccine after recovery are eligible to donate only if they:

1) had symptoms of COVID-19 and a positive test result from a diagnostic test approved, cleared, or authorized by FDA, AND
2) received the COVID-19 vaccine after diagnosis of COVID-19, AND
3) are within 6 months after complete resolution of COVID-19 symptoms

- Individuals who received a nonreplicating, inactivated, or mRNA-based COVID-19 vaccine can donate blood without a waiting period
- Individuals who received a live-attenuated viral COVID-19 vaccine should refrain from donating blood for at least 14 days after receipt of the vaccine
- Individuals who are uncertain about which COVID-19 vaccine was administered should refrain from donating blood for at least 14 days after receipt of the vaccine

Emergency Use/Compassionate Use Authorization

- Use of CP under compassionate use should be a joint decision among the clinical team managing the patients
- Compassionate use eligibility criteria for individual patients should include:
  1. Patient with laboratory confirmed COVID-19
  2. Moderate or severe disease (as defined below) with CPT given early in the course of the disease. Early in the course of disease generally means prior to respiratory failure requiring intubation and mechanical ventilation.

Moderate Disease	*Severe Disease*
• Evidence of lower respiratory disease during clinical assessment or imaging • Oxygen saturation (SpO_2) ≥94% on room air at sea level	• Dyspnea • Respiratory rate ≥30/min • Oxygen saturation (SpO_2) ≤93% • PaO2/FiO2 ratio <300 and/or • Lung infiltrates >50%

  3. Within 14 days from onset of symptoms with maximum benefit if given within 72 hours of onset of symptoms. The therapeutic window may be longer when CP is administered to patients with clinical or laboratory evidence of impaired humoral immunity.
  4. Must be able to provide informed consent. If a patient cannot provide consent, next of kin or legal surrogate decision maker should provide consent.
- Due to lack of evidence for benefit, use of CPT among patients with life-threatening disease (as defined below) is no longer recommended.

Life-threatening Disease
• Respiratory failure • Septic shock and/or • Multiple organ dysfunction or failure

- Currently there is a lack of data on the utility of antibody titer testing for recipients. Use of antibody titer levels as a guide for possible prioritization and/or screening of CPT recipients is left to the discretion of the team managing the patient.

ADMINISTRATION/CLINICAL DOSING

- Clinical dosing may first consider starting with one convalescent plasma unit, with administration of additional convalescent plasma units based on the clinical team's medical judgment and the patient's clinical response.
- Multiple doses of units with below cut off antibody titer levels is not recommended.
- Infusion should be at least 1.5 to 2 hrs.
- CPT should be administered for hospitalized or admitted patients only. Patients should be adequately monitored during and immediately after infusion.

References

US FDA (2021). Recommendations for Investigational COVID-19 Convalescent Plasma. https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma

Joyner MJ, Carter RE, Senefeld JW, Klassen SA, et al. Convalescent Plasma Antibody Levels and the Risk of Death from Covid-19. NEJM. Jan 13 2021. DOI: 10.1056/NEJMoa2031893

Libster R, Perez MG, Wappner D, Coviello S, et al. Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults. NEJM. Jan 6 2021. DOI: 10.1056/NEJMoa2033700

Simonovich VA, Burgos Pratx LD, Scibona P, et al. A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia. N Engl J Med. 2021 Feb 18;384(7):619-629. DOI: 10.1056/NEJMoa2031304.